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Search Results -

Term	Documents
(11 NOT 12).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	4
(L11 NOT L12).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	4

Database: US Patents Full Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L13

Refine Search

Recall Text | Clear

Search History

DATE: Tuesday, November 18, 2003 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ			
L13	L11 not l12	4	L13
L12	L11 and (coil or probe)	8	L12
L11	L9 and (fused with silica)	12	L11
L10	L9 and (microcoil or micro-coil or "micro coil")	0	L10
L9	L8 and (PEEK or polyetheretherketone or poly-ether-ether-ketone)	94	L9
L8	L1 and (polytetrafluoroethylene or poly-tetra-fluoro-ethylene)	2673	L8
L7	L3 and (polytetrafluoroethylene or poly-tetra-fluoro-ethylene)	0	L7
L6	L4 and (polytetrofluoroethylene or poly-tetro-fluoro-ethylene)	1	L6
L5	L4 and (polytetrafluoroethylene or poly-tetra-fluoro-ethylene)	0	L5
L4	L3 and (fused with silica)	3	L4
L3	L2 and (microcoil or micro-coil or "micro coil")	5	L3
L2	L1 and (PEEK or polyetheretherketone or poly-ether-ether-ketone)	447	L2
L1	((magnetic adj resonance) or MRI or NMR)	160257	L1

END OF SEARCH HISTORY

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Search Results - Record(s) 1 through 1 of 1 returned.

☐ 1. Document ID: US 20020149369 A1

L6: Entry 1 of 1 File: PGPB Oct 17, 2002

PGPUB-DOCUMENT-NUMBER: 20020149369
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020149369 A1

TITLE: Microfluidic device with multiple microcoil NMR detectors

PUBLICATION-DATE: October 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Peck, Tim L.	Mahomet	IL	US	
Olson, Dean	Champaign	IL	US	
Norcross, Jim	Champaign	IL	US	
Strand, David	Sherborn	MA	US	
Sweedler, Jonathan	Urbana	IL	US	

US-CL-CURRENT: 324/321; 324/306, 435/4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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Term	Documents
POLYTETROFLUOROETHYLENE	149
POLYTETROFLUOROETHYLENES	1
POLY-TETRO-FLUORO-ETHYLENE	0
POLY-TETRO-FLUORO-ETHYLENES	0
((POLY-TETRO-FLUORO-ETHYLENE OR POLYTETROFLUOROETHYLENE) AND 4).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	1
(L4 AND (POLYTETROFLUOROETHYLENE OR POLY-TETRO-FLUORO-ETHYLENE)).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	1

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Search Results - Record(s) 1 through 8 of 8 returned.

☐ 1. Document ID: US 6649415 B1

L12: Entry 1 of 8 File: USPT Nov 18, 2003

US-PAT-NO: 6649415
DOCUMENT-IDENTIFIER: US 6649415 B1

TITLE: Methods for screening compound libraries

DATE-ISSUED: November 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hindsgaul; Ole	Edmonton, Alberta		T6C 0X3	CA
Schriemer; David C.	Calgary, Alberta		T1Y 2C7	CA

US-CL-CURRENT: 436/161; 210/198.2, 210/656, 250/281, 250/282, 422/70, 435/7.1, 435/7.2, 435/DIG.14, 435/DIG.15, 435/DIG.16, 435/DIG.17, 435/DIG.18, 436/173, 436/501, 436/518

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 6627453 B1

L12: Entry 2 of 8 File: USPT Sep 30, 2003

US-PAT-NO: 6627453
DOCUMENT-IDENTIFIER: US 6627453 B1

TITLE: Methods for screening compound libraries

DATE-ISSUED: September 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hindsgaul; Ole	Edmonton, Alberta		T6C 0X3	CA
Schriemer; David C.	Calgary, Alberta		T1Y 5C7	CA

US-CL-CURRENT: 436/161; 210/198.2, 210/656, 250/281, 250/282, 422/70, 435/7.1, 435/7.2, 435/DIG.14, 435/DIG.15, 435/DIG.16, 435/DIG.17, 435/DIG.18, 436/173, 436/501, 436/518

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: US 6613575 B1

L12: Entry 3 of 8 File: USPT Sep 2, 2003

US-PAT-NO: 6613575
DOCUMENT-IDENTIFIER: US 6613575 B1

TITLE: Methods for screening compound libraries

DATE-ISSUED: September 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hindsgaul; Ole	Edmonton		T6C 0X3	CA
Schriemer; David C.	Calgary		T1Y 2C7	CA

US-CL-CURRENT: 436/161; 210/198.2, 210/656, 250/281, 250/282, 422/70, 435/7.1, 435/7.2, 435/DIG.14, 435/DIG.15, 435/DIG.16, 435/DIG.17, 435/DIG.18, 436/173, 436/501, 436/518

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 4. Document ID: US 6607921 B1

L12: Entry 4 of 8 File: USPT Aug 19, 2003

US-PAT-NO: 6607921
DOCUMENT-IDENTIFIER: US 6607921 B1

TITLE: Methods for screening compound libraries

DATE-ISSUED: August 19, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hindsgaul; Ole	Edmonton, Alberta		T6C 0X3	CA
Schriemer; David C.	Calgary, Alberta		T1Y 2C7	CA

US-CL-CURRENT: 436/161; 210/198.2, 210/656, 250/281, 250/282, 422/70, 435/7.1, 435/7.2, 435/DIG.14, 435/DIG.15, 435/DIG.16, 435/DIG.17, 435/DIG.18, 436/173, 436/501, 436/518

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 5. Document ID: US 6395169 B1

L12: Entry 5 of 8 File: USPT May 28, 2002

US-PAT-NO: 6395169
DOCUMENT-IDENTIFIER: US 6395169 B1

TITLE: Apparatus for screening compound libraries

DATE-ISSUED: May 28, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hindsgaul; Ole	Edmonton			CA
Schriemer; David C.	Edmonton, Alberta			CA

US-CL-CURRENT: 210/198.2; 210/143, 210/656, 210/659, 422/70

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 6. Document ID: US 6387257 B1

L12: Entry 6 of 8 File: USPT May 14, 2002

US-PAT-NO: 6387257
DOCUMENT-IDENTIFIER: US 6387257 B1

TITLE: Apparatus for screening compound libraries

DATE-ISSUED: May 14, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hindsgaul; Ole	Edmonton, Alberta			CA
Schriemer; David C.	Edmonton, Alberta			CA

US-CL-CURRENT: 210/198.2; 210/143, 210/656, 210/659, 422/70

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 7. Document ID: US 6355163 B2

L12: Entry 7 of 8 File: USPT Mar 12, 2002

US-PAT-NO: 6355163
DOCUMENT-IDENTIFIER: US 6355163 B2

TITLE: Apparatus for screening compound libraries

DATE-ISSUED: March 12, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hindsgaul; Ole	Edmonton, Alberta			CA
Schriemer; David C.	Calgary			CA

US-CL-CURRENT: 210/198.2; 210/143, 210/656, 210/659, 422/70

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 8. Document ID: US 6054047 A

L12: Entry 8 of 8 File: USPT Apr 25, 2000

US-PAT-NO: 6054047
DOCUMENT-IDENTIFIER: US 6054047 A

TITLE: Apparatus for screening compound libraries

DATE-ISSUED: April 25, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hindsgaul; Ole	Edmonton			CA
Schriemer; David C.	Edmonton			CA

US-CL-CURRENT: 210/198.2; 210/143, 210/656, 422/70

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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Term	Documents
COIL	769527
COILS	245205
PROBE	266940
PROBES	115308
(11 AND (PROBE OR COIL)).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	8
(L11 AND (COIL OR PROBE)).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	8

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L4: Entry 3 of 3 File: USPT Feb 15, 2000

DOCUMENT-IDENTIFIER: US 6026316 A
**** See image for Certificate of Correction ****
TITLE: Method and apparatus for use with MR imaging

Abstract Text (1):
The invention is an apparatus and method for targeted drug delivery into a living patient using magnetic resonance (MR) imaging. The apparatus and method are useful in delivery to all types of living tissue and uses MR Imaging to track the location of drug delivery and estimating the rate of drug delivery. An MR-visible drug delivery device positioned at an target site (e.g., intracranial delivery) delivers a diagnostic or therapeutic drug solution into the tissue (e.g., the brain). The spatial distribution kinetics of the injected or infused drug agent are monitored quantitatively and non-invasively using water proton directional diffusion MR imaging to establish the efficacy of drug delivery at a targeted location.

Brief Summary Text (3):
This invention relates to the design, construction, and use of magnetic resonance (MR) imaging to identify areas within a patient where changes in a molecular environment are occurring, as from chemical concentration changes effected by medical procedures. The invention also describes a drug delivery device for targeted drug delivery into a patient using magnetic resonance (MR) imaging combined with conventional catheter placement techniques, particularly including neurosurgical or neuroradiologic techniques used in intracranial drug delivery.

Brief Summary Text (5):
Although endoscopic, arthroscopic, and endovascular therapies have produced significant advances in healthcare, the diagnostic accuracy and clinical utility of these procedures is ultimately "surface limited" by what the surgeon can see through the device itself or otherwise visualize during the course of the procedure. Magnetic Resonance (MR) imaging, by comparison, overcomes this limitation by enabling the surgeon to non-invasively visualize tissue planes beyond the surface of the tissue under direct evaluation. Moreover, MR imaging enables differentiation of normal from abnormal tissues, and can display critical structures such as blood vessels in three dimensions. Thus, high-speed MR-guided therapy offers an improved opportunity to maximize the benefits of minimally invasive procedures. Prototype high-speed MR imagers which permit continuous real-time visualization of tissues during surgical and endovascular procedures have already been developed. Recent publications in the medical literature have described a number of MR-guided interventions including needle biopsies, interstitial laser therapy, interstitial cryotherapy and interstitial focused ultrasound surgery.

Brief Summary Text (8):
An important issue in targeted drug delivery is the accuracy of the navigational process used to direct the movement of the drug delivery device. Magnetic resonance imaging will likely play an increasingly important role in optimizing drug treatment of neurological disorders. One type of MR unit designed for image-guided therapy is arranged in a "double-donut" configuration, in which the imaging coil is split axially into two components. Imaging studies are performed with this system with the surgeon standing in the axial gap of the magnet and carrying out procedures on the patient. A second type of high-speed MR imaging system combines high-resolution MR imaging with conventional X-ray fluoroscopy and digital subtraction angiography

(DSA) capability in a single hybrid unit. Both of these new generations of MR scanners provide frequently updated images of the anatomical structures of interest. This real-time imaging capability makes it possible to use high-speed MR imaging to direct the movement of catheters and other drug delivery vehicles to specific tissue locations, and thereby observe the effects of specific interventional procedures.

Brief Summary Text (9):
A prerequisite for MRI-guided drug delivery into the brain parenchyma, cerebral fluid compartments, or cerebral vasculature is the availability of suitable access devices. U.S. Pat. No. 5,571,089 to Crocker et al. and U.S. Pat. No. 5,514,092 to Forman et al. disclose endovascular drug delivery and dilatation drug delivery catheters which can simultaneously dilate and deliver medication to a vascular site of stenosis. U.S. Pat. No. 5,171,217 to March describes the delivery of several specific compounds through direct injection of microcapsules or microparticles using multiple-lumen catheters, such as disclosed by Wolinsky in U.S. Pat. No. 4,824,436. U.S. Pat. No. 5,580,575 to Unger et al. discloses a method of administering drugs using gas-filled liposomes comprising a therapeutic compound, and inducing the rupture of the liposomes with ultrasound energy. U.S. Pat. No. 5,017,566 to Bodor discloses redox chemical systems for brain-targeted drug delivery of various hormones, neurotransmitters, and drugs through the intact blood-brain barrier. U.S. Pat. No. 5,226,902 to Bae et al. and U.S. Pat. No. 4,973,304 to Graham et al. disclose drug delivery devices, in which biologically active materials present within a reversibly permeable hydrogel compartment can be delivered into tissues by various endogenous and exogenous stimuli. U.S. Pat. No. 5,167,625 to Jacobsen et al. discloses an implantable drug delivery system utilizing multiple drug compartments which are activated by an electrical circuit. U.S. Pat. No. 4,941,874 to Sandow et al. discloses a device for the injection of implants, including drug implants that may used in the treatment of diseases. U.S. Pat. Nos. 4,892,538, 4,892,538, 5,106,627, 5,487,739 and 5,607,418 to Aebischer et al. disclose implantable drug therapy systems for local delivery of drugs, cells and neurotransmitters into the brain, spinal cord, and other tissues using delivery devices with a semipermeable membrane disposed at the distal end. U.S. Pat. No. 5,120,322 to Davis et al. describes the process of coating the surface layer of a stent or shunt with lathyrogenic agent to inhibit scar formation during reparative tissue formation, thereby extending exposure to the drug agent. U.S. Pat. Nos. 4,807,620 to Strul and 5,087,256 to Taylor are examples of catheter-based devices which convert electromagnetic Rf energy to thermal energy. Technology practiced by STS Biopolymers (Henrietta, N.Y.) allows incorporation of pharmaceutical agents into thin surface coatings during or after product manufacture. The invention disclosed by STS Biopolymers allows for the drugs to diffuse out of the coating at a controlled rate, thereby maintaining therapeutic drug levels at the coating surface while minimizing systemic concentrations. The coating can incorporate natural or synthetic materials that act as antibiotics, anticancer agents, and antithrombotics, according to the issued patent. U.S. Pat. No. 5,573,668 to Grosh et al. discloses a microporous drug delivery membrane based on an extremely thin hydrophilic shell. U.S. Pat. No. 5,569,197 to Helmus et al. discloses a drug device guidewire formed as a hollow tube suitable for drug infusion in thrombolytic and other intraluminal procedures.

Brief Summary Text (13):
Although U.S. Pat. No. 5,470,307 to Lindall describes significant improvements over previous catheter-based drug delivery systems, there are nonetheless some problems. First, in common with other currently used endovascular access devices, such as catheters, microcatheters, and guidewires, the catheter tip is difficult to see on MRI because of inadequate contrast with respect to surrounding tissues and structures. This makes accurate localization difficult and degrades the quality of the diagnostic information obtained from the image. Also, the mere observation of the location of the catheter in the drug delivery system does not reliably or consistently identify the position, movement and/or efficient delivery of drugs provided through the system. Thus, one objective of this invention is to provide for an MR-compatible and visible device that significantly improves the efficacy and safety of drug delivery using MR guidance.

Brief Summary Text (14):
Any material that might be added to the structure of a pliable catheter to make it MR visible must not contribute significantly to the overall magnetic susceptibility

of the catheter, or imaging artifacts could be introduced during the MR process. Moreover, forces might be applied to such a catheter by the superconducting magnetic manipulation coils of a nonlinear magnetic stereotaxis system which might be used in the practice of the present invention. In either case, the safety and efficacy of the procedure might be jeopardized, with resulting increased risk to the patient. Also, an MR-visible catheter must be made of material that is temporally stable and of low thrombolytic potential if it is to be left indwelling in either the parenchymal tissues or the cerebral vasculature. Examples of such biocompatible and MR-compatible materials which could be used to practice the invention include elastomeric hydrogel, nylon, teflon, polyamide, polyethylene, polypropylene, polysulfone, ceramics, cermets steatite, carbon fiber composites, silicon nitride, and zirconia, plexiglass, and poly-ether-ether-ketone .

Brief Summary Text (17):
MRI enables image-guided placement of a catheter or other drug delivery device at targeted intracranial loci. High-resolution visual images denoting the actual position of the drug delivery device within the brain would be extremely useful to the clinician in maximizing the safety and efficacy of the procedure. Drug delivery devices, such as catheters, that are both MR-visible and radio-opaque could be monitored by both X-ray fluoroscopy and MR imaging, thus making intra-operative verification of catheter location possible.

Brief Summary Text (20):
Exemplary of methods for active MR visualization of implanted medical devices is U.S. Pat. No. 5,211,165 to Dumoulin et al., which discloses an MR tracking system for a catheter based on transmit/receive microcoils positioned near the end of the catheter by which the position of the device can be tracked and localized. Applications of such catheter-based devices in endovascular and endoscopic imaging have been described in the medical literature, for example, Hurst et al., Mag. Res. Med., 24, 1992, pp. 343-357, Kantor et al., Circ. Res., 55, 1984, pp. 55-60; Kandarpa et al., Radiology, 181, 1991, pp. 99; Bornert et al., Proc. ISMRM, 3, 1997, p. 1925; Coutts et al., Proc. ISMRM, 3, 1997, p. 1924; Wendt et al., Proc, ISMRM, 3, 1997, p. 1926; Langsaeter et al., Proc. ISMRM, 3, 1997, p. 1929; Zimmerman et al., Proc. ISMRM, 3, 1997, p. 1930; and, Ladd et al., Proc. ISMRM, 3, 1997, p. 1937.

Brief Summary Text (23):
Magnetic Resonance Imaging (MRI) is used in combination with 1) an MR observable delivery device or 2) an MR observable medical device which can alter a water based molecular environment by performed medical operations, the delivery device or medical device being used in the presence of MR observable (in water, body fluid or tissue) compound(s) or composition(s). MRI images are viewed with respect to a molecular environment to determine the position of the delivery or medical device (hereinafter collectively referred to as the "delivery device" unless otherwise specifically identified) and changes in the environment where the delivery device is present as an indication of changes in the molecular environment. As the delivery of material from the delivery device is the most significant event within the molecular environment in the vicinity of the delivery area, the changes in the molecular environment are attributable to the delivery of the MR observable compounds or compositions. Changes in signal intensity within the MR images reflect the changes in the molecular environment and therefore track the location of delivered materials, and are indicative of delivery rates and delivery volumes in viewable locations. With the medical device, chemical composition within the molecular environment may also be altered as by the removal of deposits of certain materials into the liquid (water) environment, where those materials can alter the MR response. Some materials which may be removed by medical procedures will not affect the MR response, such as calcium, but fatty materials may. Additionally, medical treatments which stimulate natural activities of chemical producing systems (e.g., the glands, organs and cells of the body which generate chemicals such as enzymes and other chemicals with specific biological activity [e.g., dopamine, insulin, etc.] can be viewed under direct MR observation and any changes in chemical synthetic activity and/or delivery can be seen because of molecular environment changes which occur upon increased synthetic activity.

Brief Summary Text (25):
While the ADC is the preferred means within the present invention of mapping the

delivery of drug in tissue, other embodiments of the invention allow for additional tissue contrast parameters to track the delivery of a drug into tissue. In other words, the delivery of a drug into tissue will cause other MRI-observable changes which can be mapped (as is done for ADC) and which can be used to spatially track the delivery and extent of a drug into a tissue. While some of these observations may be larger in magnitude than others, any of the effects can be used as a tracking mechanism.

Brief Summary Text (27):
MR imaging of the alterations in the B0 magnetic field (also known as imaging of the local magnetic susceptibility) can reveal the spatial distribution of a drug from the interaction of the drug with the otherwise homogeneous magnetic field found in MRI. To enhance the alterations in the magnetic field B0 caused by the drug, small amounts of a B0-altering added agents can be added to the drug during delivery. This can include iron oxide particles, or materials comprising lanthanide-, manganese-, and iron-chelates. In addition, vehicles containing differing gases (N2, O2, CO2) will also alter the local magnetic field and thus produce a magnetic susceptibility effect which can be imaged.

Brief Summary Text (28):
The invention includes a device and a method for MR-guided targeted drug delivery into a patient, such as intracranial drug delivery, intraspinal drug delivery, intrarenal drug delivery, intracardial drug delivery, etc. The MR-visible drug delivery device is guided to target entrance points to the patient such as periventricular, intracerebroventricular, subarachnoid, or intraparenchymal tissues magnetic resonance imaging, or conventional methods of neurosurgical or neuroradiologic catheter manipulation. The drug delivery device has a linearly arranged array of radiopaque and MR-visible markers disposed at its distal end to provide easily identifiable reference points for trackability and localization under susceptibility MR imaging and X-ray fluoroscopy guidance. Additionally, active MR visualization of the drug delivery device is achieved by means of RF microcoils positioned along the distal axis of the device. MR visibility can be variably adjustable based on requirements related to degree of signal intensity change for device localization and positioning, enhancement along the shaft of the device, enhancement around the body of the device, visibility of the proximal and distal ends of the device, degree of increased background noise associated with device movement, and other factors which either increase or suppress background noise associated with the device. Since the tip of the drug delivery device can be seen on MR and X-ray images and thus localized within the brain, the multiple point source locations of drug delivery are therefore known and can be seen relative to the tip or the shaft of the device.

Brief Summary Text (29):
Targeted delivery of drug agents is performed utilizing MR-compatible pumps connected to variable-length concentric MR-visible dialysis probes each with a variable molecular weight cut-off membrane, or by another MR-compatible infusion device which injects or infuses a diagnostic or therapeutic drug solution. Imaging of the injected or infused drug agent is performed by MR diffusion mapping using the RF microcoils attached to the distal shaft of the injection device, or by imaging an MR-visible contrast agent that is injected or infused through the walls of the dialysis fiber into the brain. The delivery and distribution kinetics of injections or infusions of drug agents at rates between 1 ul/min to 1000 ul/min are monitored quantitatively and non-invasively using real-time contrast-enhanced magnetic susceptibility MR imaging combined with water proton directional diffusion MR imaging.

Drawing Description Text (5):
FIG. 4 is a further cross-sectional view of the preferred embodiment of the device which shows the disposition of RF microcoil elements along the distal shaft of the delivery device.

Drawing Description Text (7):
FIGS. 6A, 6B and 6C are side elevational views of the preferred embodiment of the device illustrating the relationship between the RF microcoils and individual tubular components of the distal tip of each drug delivery catheter.

Detailed Description Text (4):
The basic operation of the present invention therefor involves the initial MR imaging observation of a molecular environment of a patient (e.g., a particular area or region of a patient, such as tissue, particularly such tissue as that present in organs or systems of animal bodies and especially the human body, including, but not limited to the intracranial compartment and the various anatomic regions of the brain, including the cerebral ventricles, cisterns, epidural and subdural spaces, sinuses, and blood vessels, the spinal cord, including disks, nerves and associated vascular system, the heart and the coronary vascular circulation, liver and the hepatic vascular circulation, kidney and the renal vascular circulation, spleen and the splenic vascular system, gastrointestinal system, special senses, including the visual system, auditory system, and olfactory system endocrine system including the pituitary gland, thyroid gland, adrenal gland, testes, and ovaries, with observation of an MR image signal intensity at a given time and/or state (e.g., prior to material introduction or at some defined stage of material diffusion into the molecular environment. In an example of the method of the invention, the distribution of the material in the tissue is determined by releasing an amount of the material through a drug delivery device positioned in the tissue, allowing the material to diffuse in the tissue, and analyzing the resulting MR signal intensity. On a continual basis or at some subsequent time interval later (e.g., a pulsed interval, preselected interval, random interval, frequent or sporadic intervals), the MR image of the molecular state within the same general area is observed. Changes in the characteristics, properties or quality of the image, such as the image signal intensity within the area are presumptively (and in most cases definitively) the result of the introduction of material into the original molecular environment and alteration of the MR response for regions of the environment where delivered material concentration has changed. By repeating observation of the MR image signal intensity within an area at least once (e.g., first taking the initial observation at a material concentration state at a time T.sub.1, and at least one subsequent observation of MRI-observable changes such as in the signal intensity qualities at a time T.sub.2), the change in MR image signal intensity qualities can be related to the change in material concentration between times T.sub.1 and T.sub.2, whether that change is from a starting point of zero concentration or from an existing concentration level. The observations therefore relate to the actual delivery of material into the molecular environment in an observable, and to some lesser degree, quantifiable manner.

Detailed Description Text (32):
With further reference to FIGS. 1-3 of the drawings, the outlet tubing 2a is incorporated into the probe into the dialysis chamber 1 via a small perforation in the inlet tubing. The entire upper portion of the assembly, including the junction between the inlet tubing and plastic cannula, is sealed with epoxy. The outer tubing consists of 5-10 cm length of flexible fused silica tubing (Polymicro Technologies). These probes are inexpensive and easy to construct, and the small o.d. minimizes the tissue damage. The concentric design makes it simple to implant the probe into different intracranial locations.

Detailed Description Text (33):
With reference to FIG. 4, active MR visualization of drug delivery is achieved by means of one or more RF microcoils 9, 9a, 10, 10a positioned along the longitudinal axis of the device 4. Particularly preferred is an RF coil consisting of a circular loop of gold or other conductive material 9 positioned around the widest part of the drug delivery device, which would project the field-of vision (FOV) furthermost into the tissue. Depending on orientation of the coil with the magnetic B0, single microcoils may be used separately or may be constructed in an array that may be used together to optimally image the surrounding tissue structure and contrast. In order to reduce the thickness of the RF microcoil, the coil material is sputter-coated onto the surface of the drug delivery device. Preferred also for very small (nanoliter or microliter) injections is a solenoid volume RF microcoil 9a, which by design is sensitive only to the volume inside the coil, said imaging volume being directly related to the diameter of the RF coil. Another preferred MR imaging method which can be used to practice the invention is a combination of RF microcoil and surface coil positioned on the surface of the patient's head. Also preferred is telescoping coil 10 inside of the catheter, expanding it when one wants to image and

then withdraw the coil and move on. One may see several cm with this idea. Another preferred method of MR imaging involves the use of an oblong surface loop of wire at the end of a slanted drug delivery device or along the shank of the device, thereby yielding a long FOV. In each of these preferred embodiments of the invention, the transmitting coil would be the head or body volume RF coil inside of the MR imager. The RF surface coil is used only for detection purposes. In another preferred embodiment, a preamplifier 10b positioned near the distal end of the delivery device 4 serves to amplify signals from the RF microcoils 9, 91, 10, 10a.

Detailed Description Text (34):
With further reference to FIGS. 3 and 4, the medical device used in the preferred practice of the present invention for delivery of materials may vary widely with respect to its structure, being highly dependent upon the particular procedural use to which it is being intended. However, there are many features which can be common to all of the devices or which should at least be considered in the various constructions. The simplest device could be a single delivery tube (catheter) which has MR responsive material in or on the composition of the tubing 19, preferably near the distal end or outlet of the delivery tube for assisting in detection by the MR imaging system. The next level of simplified construction would be the presence of MR coils or microcoils 9, 9a, 10, 10a at or near the distal end of the catheter. This again, as elsewhere described, improves the visibility of the viewable signal observable by the MRI system. More than one coil or microcoil may be present, as the distribution of microcoils along a length of the catheter helps define the region within which local signals are detected at efficient intensities. That is, each coil acts as a detector of local MR intensity, and each coil supports a volume around the coil which is observable by MRI systems. The coils may add or integrate their detectable volumes, defining a combined volume which can be efficiently observed by the MR system. As different medical procedures are performed in different environments, with different shapes and different variations in densities, the coils may be located, sized, angled, or otherwise designed to provide specific MR signals and/or responses tailored to the anticipated needs of a particular procedure. In general, the invention is best practiced by employing an array of RF microcoils, such that an image is obtained for any orientation of the drug delivery device.

Detailed Description Text (37):
One type of configuration which is presently considered as the preferred embodiment of the invention is the use of a core of element(s) surrounded by a sheath or distribution of additional elements. For example, with further reference to FIGS. 3A and 3B, a central core element my comprise a single tube for delivery of a material, a pair of tubes for delivery of two chemicals, a delivery and withdrawal tube, or a procedurally inert structural support element 11. Around the central core element may be disposed multiple additional elements 21-27, usually seeking as near to a circular distribution about the central core as geometries allow. The attempt at the circular distribution is primarily for purposes of optimizing a small size for the diameter of the article, and is not necessarily a functional aspect to the performance of the device. With respect to FIG. 5, the MR responsive materials, including MR microcoils, may be located within the central core 33, around the central core 34 (beneath any next layering of elements), or over the elements surrounding the central core 34a. Where one or more of the elements receive, transmit or are powered by electrical signals, it is desirable that these elements be electrically separated by either or both of physical separation or additional insulation to prevent mixing or cross-transmission of signals between the distinct elements. Carrying and withdrawing tubes (as well as other elements) may also secondary functions. For example, a carrying tube may be conductive (by being naturally conductive or by having a conductive coating in or outside of the tube) and the electrical connection may be associated with an electronic element or component at the distal end of the device. The tube may thereby act as a carrying tube and electrical connection to the electronic component or element. Structural or adhesive support materials between different elements may also provide such functions. The system may have the material delivery device comprise a catheter assembly of from 2 to 10 mass transporting elements.

Detailed Description Text (39):
With reference to FIG. 6a, in another embodiment the dialysis probe is replaced by an MR-visible microcatheter 38, which is a single extrusion catheter made from one

of several possible sizes of a polyethylene terephthalate proximal shaft, e.g. 30 ga. The 1-2.dagger. mm distal segment of the microcatheter drug delivery device is made of elastomeric hydrogel or similar soft material which minimizes tissue damage during insertion. A plurality of semipermeable membranes 38b are placed circumferentially at regular intervals along the distal segment of the microcatheter, thus enabling wide dispersion of an injected agent, semipermeable membrane consisting of a 0.18-0.22 m.mu. millipore filter. The companion microguidewire in this example is made of nitinol or similar memory metal which enables directed placement of the tip of the catheter. The microguidewire 37 is threaded into a clear hub luek-lock cap 39 made of poly-methel-pentene or similar compatible plastic. Both the catheter and guidewire have a linearly arranged array of radiopaque and MR-visible markers 40 disposed at the distal end to provide easily identifiable reference points for trackability and localization under MR imaging and X-ray fluoroscopy guidance. The microcatheter can also be made from any of the well-known soft, biocompatible plastics used in the catheter art such as Percuflex, a trademarked plastic manufactured by Boston Scientific Corporation of Watertown, Mass. With further reference to FIG. 6a of the drawings, when the delivery device is positioned intracranially, the distal markers will be identifiable in an MR image and by X-rays. In another preferred embodiment, two or more RF microcoils are placed along the distal shaft of the microcatheter.

Detailed Description Text (41):
In another embodiment of the invention, the MR-visible solution contains sterically stabilized liposomes, with lipophilic or hydrophilic chelators, such as polyaminocarboxylic acids and their salts, such as DTPA on phosphatidyl ethanolamine or steric acid embedded within the external bilayer, or double-label liposomes that chelate a T2-sensitive metal ion within the internal aqueous space and another T1-sensitive metal ion on the outside membrane surface, or liposomes which contain 100-1000 nm air-bubbles, such as argon, carbon dioxide, or air, as a contrast agent In another preferred embodiment, RF microcoils 41a-f are positioned at the distal ends of individual delivery tubes, said microcoils acting as local MR detectors.

Detailed Description Text (45):
Methods to obtain absolute measurements of ADC using MR imaging have been described in the medical literature, for example, Moseley et al., Mag. Res. Med., 19, 1991, pp. 321-326, and Moseley et al., Topics Mag. Res. Med., 3, 1991, pp. 50-68). It is well established that if there is restriction to diffusion (e.g. from cell walls), then the measured ADC will decrease with increasing diffusion time. Thus, an express objective of the present invention is to evaluate the efficacy of MR image-guided drug delivery by measuring restricted diffusion with localized MR pulse sequences. In the method of the present invention, modeling of restricted diffusion is used to estimate the size of the diffusion spaces and the permeability of the barriers to drug agents injected into the brain microenvironment. A conventional imaging sequence is repeated with field gradients of increasing strength or duration. The signal decays away exponentially as e-bD, where b depends on the strength, duration and timing of the diffusion-sensitizing gradients. However, the diffusion gradients make the sequence extremely sensitive to motion. Thus, in a preferred embodiment of the invention, a navigator echo technique, or its variants, are used to suppress the contaminating effects of patient motion on the ADC measured with MR imaging. In another preferred embodiment, high speed echoplanar imaging is used without movement artifact. In a further preferred embodiment of the present invention, localized measurements of the ADC, .DELTA.B0, T1, T2, MTC, chemical shift frequency, and temperature are acquired from images produced from single-shot or multi-shot stimulated echo (STEAM), gradient echo (GRE or FLASH), or fast spin-echo (FSE) MRI sequences.

Other Reference Publication (5):
Hurst, G.C., et al., "Intravascular (Catheter) NMR Receiver Probe: Preliminary Design Analysis and Application to Canine Iliofemoral Imaging", Mag. Res. Med., 24, 343-357, (1992).

Other Reference Publication (8):
Moseley, M.E., et al., " Magnetic resonance imaging of diffusion and perfusion", Top Mag. Reson. Imaging, 3(3), 50-67, (1991).

Other Reference Publication (12):
Wimberger, D.M., et al., "Identification of "Premyelination" by Diffusion-Weighted MRI", J. of Computer Assisted Tomography, 19(1), 28-33, (1995).

CLAIMS:

1. A method for observing the delivery of material to tissue in anatomic regions of the brain of a living patient comprising the steps of:

a) observing in real time by Magnetic Resonance Imaging a visible image within an area or volume comprising tissue in the anatomic region of the brain of said living patient, said area or volume including a material delivery device,

b) delivering at least some material by said material delivery device into said area or volume comprising tissue of a living patient while observing said visible image in real time,

c) observing in real time a change in amplitude of a Magnetic Resonance signal of said visible image of an area or volume comprising tissue of a living patient while said material delivery device is still present within said area or volume within said anatomic region of the brain.

15. A method for observing the increase of material within aqueous environments or tissue in the anatomic region of the brain in a living patient comprising the steps of:

a) observing in real time by Magnetic Resonance Imaging a visible image within an area or volume comprising tissue in the anatomic region of the brain of said living patient, said area or volume including a medical device which can be observed by Magnetic Resonance Imaging,

b) causing by said medical device at least some therapeutic material which causes an alteration in the magnetic response of water in which said material is dispersed or dissolved to increase its concentration within said area or volume comprising an aqueous environment or tissue in the anatomic region of the brain of a living patient while observing said visible image in real time,

c) observing in real time a change in a property of said visible image of an area or volume comprising tissue of a living patient while said medical device is still present within said volume,

d) observing in real time a change in a property of said visible image after said medical device has been moved from within said area or volume of tissue.

17. A method of observing a different rate of passage of a chemical through structural material within the body of a living patient, said material having a delivery side and a distribution side, said method comprising:

a) observing by Magnetic Resonance Imaging a visible image within an area to volume comprising tissue of said living patient, said area or volume including a delivery device which can be observed by Magnetic Resonance Imaging,

b) causing by said delivery device to deliver at least some material which causes an alteration in the magnetic response of water in which said material is dispersed or dissolved,

c) observing movement of said material within said patient through said material from said delivery side or said distribution side,

d) observing in real time a change in a property of a visible image in an area or volume on said distribution side of said material said medical device is still present within said area or volume, and

e) observing differences in rates of penetration of said chemical material through said structural material at different areas of said structural material which are

indicative of different properties in said structural material at said different areas which are evidence of a clinical condition in said structural material.

20. A method for observing the delivery of material to tissue in a living patient comprising:

a) observing by Magnetic Resonance Imaging with actively shielded gradients of at least 12 mTesla/m a visible image within an area or volume comprising tissue of said living patient, said area or volume including a material delivery device,

b) delivering at least some therapeutic material by said material delivery device into said area or volume comprising tissue of a living patient,

c) observing in real time a change in a property of said visible image of an area or volume comprising tissue of a living patient while said material delivery device is still present within said area or volume.

21. The method of claim 20 wherein said Magnetic Resonance Imaging is with actively shielded gradients of at least 20 mTesla/m.

22. The method of claim 20 wherein said Magnetic Resonance Imaging is with a magnetic field of at least about 1.5 Tesla.

23. A method for observing the delivery of material to tissue in a living patient comprising:

a) observing in real time by Magnetic Resonance Imaging with diffusion gradients of at least 600 s/mm.sup.2 a visible image within an area or volume comprising tissue of said living patient, said area or volume including a material delivery device,

b) delivering at least some pharmaceutical material by said material delivery device into said area or volume comprising tissue of a living patient,

c) observing a change in a property of said visible image of an area or volume comprising tissue of a living patient while said material delivery device is still present within said area or volume.

24. A method for observing the delivery of therapeutic material to tissue in a living patient comprising the steps of:

a) observing in real time by Magnetic Resonance Imaging a visible image within an area or volume comprising tissue of said living patient, said area or volume including a material delivery device,

b) delivering at least some therapeutic material by said material delivery device into said tissue within said area or volume comprising tissue of a living patient,

c) observing in real time a change in a property of said visible image in said tissue within said area or volume while said material delivery device is still present within said area or volume within said visible image.

27. A method for observing the delivery of material to tissue in anatomic regions of the spinal cord of a living patient comprising the steps of:

a) observing in real time by Magnetic Resonance Imaging a visible image within an area or volume comprising tissue in the anatomic region of the brain of said living patient, said area or volume including a material delivery device,

b) delivering at least some material by said material delivery device into said area or volume comprising tissue of a living patient while observing said visible image in real time,

c) observing in real time a change in amplitude of a Magnetic Resonance signal of said visible image of an area or volume comprising tissue of a living patient while said material delivery device is still present within said area or volume within

said anatomic region of the brain.